[0013] Typically, "pluripotent" stem cells are isolated and maintained on mitotically inactive feeder layers of fibroblasts. Fibroblasts are cells of mesodermal origin that make the structural fibers and ground substance of connective tissues. Feeder layers of fibroblasts perform a dual role: 1) they release nutrients into the culture medium; and 2) they provide a structural network and a surface on which ES cells can grow. It has been described that these feeder-dependent culture conditions are useful for the isolation of mouse and human ES cells, and such feeder layers have been proven to be important to maintain the ES cells in an undifferentiated state. The importance of feeder cells suggests that they provide a factor that suppresses the differentiation or promotes the self-renewal of "pluripotent" stem cells. However, only a few of such factors have been fully characterized. One of them is a leukemia inhibitory factor (LIF), which is a member of the family of cytokines related to interleukin-6.

[0014] For murine ES cells, LIF can replace the requirement for feeder cells. Importantly, activation of the signaling component of the LIF receptor, glycoprotein 130 (gp 130), is both necessary and sufficient for inhibiting murine cell differentiation. A crucial downstream effector of gp130 is the signal transducer and activator of transcription-3 (STAT3). Other signaling molecules acting downstream of gp130, such as the mitogen-activated protein kinase, seem to actually inhibit ES cell self-renewal.

[0015] In contrast to murine ES cells, the growth of human ES cells may require feeder cells, but does not seem to require LIF. Presumably, this is because the feeder cells produce multiple growth factors. Therefore, it is possible that some of the same downstream signaling molecules required for mouse ES cell growth, including STAT3, are already activated in human ES cells by other factors. The recent development of feeder-independent culture conditions for human ES cells still necessitates the use of conditioned medium from feeder cells indicating either that these cells require factors produced by feeder cells or that feeder cells remove some inhibitory factor from the culture medium. It has also been shown that the conditioned medium from a specific human tumor line contains a number of unique human stem cell growth factors including a novel ES cell growth factor significantly more potent than LIF (Minger, 2003). However, the precise nature of all of the